Amendment to the Claims

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1. (Original) A method of guiding the fate of differentiation of a cell into a specific cell type, comprising

a) providing a sample comprising the cell;

b) contacting the sample with a Groucho-interacting protein (GIP) in an amount and for a time sufficient to result in the formation of a complex between the GIP and a Groucho corepressor protein;

wherein the GIP and Groucho-corepressor protein complex represses DNA transcription and suppresses alternative pathways of differentiation, thereby guiding the fate of differentiation of the cell into a specific cell type.

2. (Original) The method of claim 1 wherein the method further comprises the step of contacting the cell with an exogenous Groucho corepressor protein.

3. (Original) The method of claim 1 wherein the Groucho corepressor protein is endogenous to the cell.

4. (Original) The method of claim 1, wherein the Groucho corepressor protein is selected from the group consisting of Grg1, Grg2, Grg3, and Grg4 and their human homologs.

5. (Original) The method of claim 1, wherein the GIP comprises a TN-like domain.

6. (Original) The method of claim 1, wherein the GIP is a homeodomain polypeptide.

7. (Original) The method of claim 6 wherein the homeodomain polypeptide is a class II homeodomain polypeptide.

8. (Original) The method of claim 7 wherein the class II homeodomain polypeptide is a member of the Nkx polypeptide family.

9. (Original) The method of claim 8, wherein the Nkx polypeptide is selected from the group consisting of Nkx2.2, Nkx2.9, Nkx6.1, Nkx6.2, and Nkx6.3 and their human homologs.

10. (Original) The method of claim 9, wherein the guided differentiation results in the cell being differentiated into a motor neuron cell.

11. (Original) The method of claim 6 wherein the homeodomain polypeptide is a class I homeodomain polypeptide.

12. (Original) The method of claim 11 wherein the class I homeodomain polypeptide is selected from the group consisting of members of the Pax, Dbx, and Irx polypeptide families.

13. (Original) The method of claim 1 wherein the cell is a stem cell.

14. (Original) The method of claim 13 wherein the cell is a neural stem cell.

15. (Original) The method of claim 1 wherein the cell is a progenitor cell.

16. (Original) The method of claim 1, wherein the specific cell type into which the cell differentiates is a neuron.

17. (Original) The method of claim 16, wherein the neuron is an interneuron, a motor neuron or a projection neuron.

18. (Original) The method of claim 17, wherein the projection neuron is selected from the group consisting of a dopaminergic neuron, a cortical neuron, a gaba-ergic neuron and a glutaminergic neuron.

19. (Original) The method of claim 1, wherein the specific cell type into which the cell differentiates is selected from the group consisting of a stem cell, a cell of the peripheral nervous system, a kidney cell, a heart muscle cell, a pancreatic cell, a skin cell, a liver cell, and a white or red blood cell.

20. (Original) The method of claim 1, wherein the GIP is selected from the group consisting of Nkx6.1, Nkx6.2, Nkx6.3, and Nkx2.2 and the cell type into which the cell differentiates is a beta cell producing insulin.

21. (Original) The method of claim 1, wherein the contacting of the sample with a GIP occurs either *in vitro*, *ex vivo*, or *in vivo*.

22. (Original) The method of claim 21, wherein the contacting of the sample with a GIP occurs either *ex vivo*.

23. (Original) The method of claim 1, wherein the GIP is a polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NO:7 and 13.

24. (Currently Amended) The method of claim 1, wherein the GIP is a polypeptide comprising the amino acid sequence X_{AA1}-X_{AA2}-X_{AA3}-X_{AA4}-X_{AA5}-X_{AA6}-X_{AA7}-X_{AA8}-X_{AA9}-X_{AA10}-X_{AA11} (SEQ ID NO:14), wherein X_{AA1} is Thr, Leu, or Ser; X_{AA2} is Gly or Pro; X_{AA3} is Phe or His; X_{AA4} is Ser, Thr, Gly, or His; X_{AA5} is Val or Ile; X_{AA6} is Lys, Arg, Asn, or Ser; X_{AA7} is Asp or Ser; X_{AA8} is Isl or Leu; X_{AA9} is Leu; X_{AA10} is Asp, Asn, Ser, or Gly; and X_{AA11} is Leu or Arg.

25. (Original) An isolated polypeptide comprising an amino acid sequence selected from the group consisting of:

(a) an amino acid sequence of SEQ ID NO:7 or 13; and

(b) a variant of an amino acid sequence of SEQ ID NO:7 or 13, wherein one or more amino acid residues in said variant differs from the amino acid sequence of said mature form, provided that said variant differs in no more than 15% of amino acid residues from said amino acid sequence.

26. (Original) The polypeptide of claim 25, wherein said polypeptide comprises the amino acid sequence of a naturally-occurring allelic variant of an amino acid sequence of SEQ ID NO:7 or 13.

27. (Original) The polypeptide of claim 26, wherein said allelic variant comprises an amino acid sequence that is the translation of a nucleic acid sequence differing by a single nucleotide from the nucleic acid sequence of SEQ ID NOS:12.

28. (Original) The polypeptide of claim 25, wherein the amino acid sequence of said variant comprises a conservative amino acid substitution.

29. (Original) An isolated nucleic acid molecule comprising a nucleic acid sequence encoding a polypeptide comprising an amino acid sequence,

wherein the amino acid sequence encoded by the nucleic acid molecule is selected from the group consisting of:

(a) the amino acid sequence of SEQ ID NO:7 or 13;

(b) a variant of an amino acid sequence of SEQ ID NO:7 or 13, wherein one or more amino acid residues in said variant differs from the amino acid sequence of said mature form, provided that said variant differs in no more than 15% of amino acid residues from said amino acid sequence; and

wherein the nucleic acid molecule is selected from the group consisting of:

(c) a nucleic acid fragment encoding at least a portion of a polypeptide comprising an amino acid sequence of SEQ ID NO:7 or 13, or a variant of said polypeptide, wherein one or more amino acid residues in said variant differs from the amino acid sequence of said mature form, provided that said variant differs in no more than 15% of amino acid residues from said amino acid sequence; and

(d) a nucleic acid molecule comprising the complement of (a), (b), or (c).

30. (Original) The nucleic acid molecule of claim 29, wherein the nucleic acid molecule comprises the nucleotide sequence of a naturally-occurring allelic nucleic acid variant.

31. (Original) The nucleic acid molecule of claim 29, wherein the nucleic acid molecule encodes a polypeptide comprising the amino acid sequence of a naturally-occurring polypeptide variant.

32. (Original) The nucleic acid molecule of claim 29, wherein the nucleic acid molecule differs by a single nucleotide from the nucleic acid of SEQ ID NO:12.

33. (Original) The nucleic acid molecule of claim 29, wherein said nucleic acid molecule comprises a nucleotide sequence selected from the group consisting of:

(a) the nucleotide sequence of SEQ ID NO:12;

(b) a nucleotide sequence differing by one or more nucleotides from the nucleotide sequence of SEQ ID NO:12, provided that no more than 20% of the nucleotides differ from said nucleotide sequence;

(c) a nucleic acid fragment of (a); and

(d) a nucleic acid fragment of (b).

34. (Original) The nucleic acid molecule of claim 29, wherein said nucleic acid molecule hybridizes under stringent conditions to the nucleotide sequence of SEQ ID NOS:12, or a complement of said nucleotide sequence.

35. (Original) The nucleic acid molecule of claim 29, wherein the nucleic acid molecule comprises a nucleotide sequence selected from the group consisting of:

(a) a first nucleotide sequence comprising a coding sequence differing by one or more nucleotide sequences from a coding sequence encoding said amino acid sequence, provided that no more than 20% of the nucleotides in the coding sequence in said first nucleotide sequence differ from said coding sequence;

(b) an isolated second polynucleotide that is a complement of the first polynucleotide; and

(c) a nucleic acid fragment of (a) or (b).

36. (Original) A vector comprising the nucleic acid molecule of claim 35.

37. (Original) The vector of claim 36, further comprising a promoter operably-linked to said nucleic acid molecule.

38. (Original) A cell comprising the vector of claim 36.

39. (Original) An antibody that binds immunospecifically to the polypeptide of claim 25.

40. (Original) The antibody of claim 39, wherein said antibody is a monoclonal antibody.

41. (Original) The antibody of claim 39, wherein the antibody is a humanized antibody.

42. (Currently Amended) A peptide less than 400 amino acids in length that includes the amino acid sequence X_{AA1}-X_{AA2}-X_{AA3}-X_{AA4}-X_{AA5}-X_{AA6}-X_{AA7}-X_{AA8}-X_{AA9}-X_{AA10}-X_{AA11} (SEQ ID NO:14), wherein X_{AA1} is Thr, Leu, or Ser; X_{AA2} is Gly or Pro; X_{AA3} is Phe or His; X_{AA4} is Ser, Thr, Gly, or His; X_{AA5} is Val or Ile; X_{AA6} is Lys, Arg, Asn, or Ser; X_{AA7} is Asp or Ser; X_{AA8} is Ile or Leu; X_{AA9} is Leu; X_{AA10} is Asp, Asn, Ser, or Gly; and X_{AA11} is Leu or Arg.

43. (Original) The peptide of claim 42, wherein said peptide is less than 100 amino acids in length.

44. (Original) The peptide of claim 42, wherein said peptide comprises the amino acid sequence of SEQ ID NO:7.

45. (Original) A purified complex comprising a first polypeptide and a second polypeptide, wherein the first polypeptide comprises a GIP and the second protein comprises a Groucho corepressor protein.

46. (Original) The complex of claim 45, wherein the first polypeptide is labeled.

47. (Original) The complex of claim 45, wherein the second polypeptide is labeled.

48. (Original) The complex of claim 47, wherein the first polypeptide is labeled.

49. (Original) The complex of claim 45, wherein the first polypeptide is selected from the group consisting of class I and class II homeodomain polypeptides.

50. (Original) The complex of claim 45, wherein the first polypeptide contains a TN domain.

51. (Original) The complex of claim 45, wherein the Groucho corepressor protein is selected from the group consisting of Grg1, Grg2, Grg3, or Grg4 and their mammalian homologs.

52. (Original) The complex of claim 45, wherein the GIP comprises a TN-like domain.

53. (Original) The complex of claim 45, wherein the GIP is a homeodomain polypeptide.

54. (Original) A purified complex comprising a first polypeptide and a second polypeptide, wherein said first polypeptide comprises a region of amino acids of a GIP sufficient to allow the first polypeptide to bind the second polypeptide, and wherein the second polypeptide comprises a region of amino acids of a Groucho corepressor protein sufficient to bind the first polypeptide.

55. (Original) A chimeric polypeptide comprising a first domain covalently linked to a second domain, wherein the first domain comprises six or more amino acids of the first polypeptide of claim 45 and the second domain comprises six or more amino acids of the second polypeptide of claim 45.

56. (Original) The chimeric polypeptide of claim 55 wherein the first domain comprises a GIP binding domain and the second domain comprises a groucho corepressor binding domain.

57. (Original) The chimeric polypeptide of claim 28, wherein the first domain comprises a TN domain.

58. (Original) A nucleic acid encoding the chimeric polypeptide of claim 55.

59. (Original) A vector comprising the nucleic acid of claim 58.

60. (Original) A cell comprising the vector of claim 58.

61. (Original) An antibody which specifically binds the complex of claim 45.

62. (Original) A kit comprising a reagent which can specifically detect the complex of claim 45.

63. (Original) The kit of claim 62, wherein the reagent is selected from the group consisting of an antibody specific for the complex, an antibody specific for the first polypeptide, and an antibody specific for the second polypeptide.

64. (Original) A method of identifying an agent which modulates the stability or activity of the complex of claim 45 comprising:

a) providing the complex:

b) contacting the complex with a test agent; and

c) detecting whether the test agent modulates the stability or activity of the complex.

65. (Original) A method of identifying an agent which disrupts a polypeptide complex, the method comprising

a) providing the complex of claim 45;

b) contacting the complex with a test agent; and

c) detecting the presence of a polypeptide displaced from the complex,

wherein the presence of displaced polypeptide indicates the agent disrupts the complex.

66. (Original) A method for the screening of a candidate substance interacting with the complex of claim 45, comprising:

a) providing the complex of claim 45;

b) obtaining a candidate substance;

c) bringing into contact the complex with the candidate substance; and

d) detecting the complexes formed between the polypeptide and the candidate substance.

67. (Original) A method for the screening of a candidate substance interacting with a Groucho-corepressor protein, comprising

a) providing a Groucho-corepressor protein;

b) obtaining a candidate substance;

c) bringing into contact the polypeptide with the candidate substance; and

d) detecting the complexes formed between the polypeptide and the candidate substance.

68. (Original) A method for inhibiting the guided differentiation of a cell resulting in the impairment of ventral patterning, the method comprising:

contacting the complex of claim 45 with an agent that disrupts the complex,

thereby inhibiting the guided differentiation by disrupting the complex, which is necessary for differentiation.

69. (Original) A method of identifying a polypeptide complex in a subject, the method comprising:

a) providing a biological sample from a subject; and
b) detecting, if present, the polypeptide complex of claim 45 in the sample, thereby identifying the complex.

70. (Original) A method of determining altered expression of a polypeptide in a subject, the method comprising

a) providing a biological sample from the subject;
b) measuring the level of the complex of claim 45 in the sample; and
c) comparing the level of the complex from step b) to the level of the complex in a reference sample whose level of the complex of claim 45 is known;

thereby determining whether the subject has altered expression of the polypeptide.

71. (Original) A method of treating or preventing a disease or disorder involving altered levels of the complex of claim 45 by administering a therapeutically effective amount of at least one molecule that modulates the function of the complex to a subject in need thereof.

RESPONSE TO NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

In response to the Notice to Comply with Sequence Requirements, Applicants have (1) amended the specification to include a sequence listing, (2) amended the specification and claims to include proper sequence ID numbers, (3) included a computer readable form of the sequence listing.

The undersign avers that the paper copy of the sequence listing is identical to the computer readable form of the sequence listing and include no new matter.